Resilience as a Research Priority
A Perspective from NIA

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NIA

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Recent NIA-Sponsored Initiatives on Resilience


• **RFA-AG-17-014**: Predictors and Determinants of Age-Related Changes in Resiliencies to Physical Stressors in Humans (UH2/UH3) [http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-17-014.html](http://grants.nih.gov/grants/guide/rfa-files/RFA-AG-17-014.html)

• **RFA-AG-17-061**: Interdisciplinary Research to Understand the Complex Biology of Resilience to Alzheimer’s Disease Risk (R01) [https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-17-061.html](https://grants.nih.gov/grants/guide/rfa-files/RFA-AG-17-061.html)


https://www.nia.nih.gov/resilienceandaging
Special Issue: Moving Geroscience Into Uncharted Waters: Perspective

Resilience in Aging Mice

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Abstract

Recently discovered interventions that target fundamental aging mechanisms have been shown to increase life span in mice and other species, and in some cases, these same manipulations have been shown to reduce health span, enhance health-related quality of life, and extend maximal age-related disease-free survival. In mice, these interventions are associated with decreases in the body’s capacity to respond to or recover from clinically relevant or age-related injuries, infections, or vascular events. It is hypothesized that the age-related increase in susceptibility to these diseases and conditions is driven by or associated with the decline in resilience. Thus, a test for resilience at middle age or even earlier could serve as a surrogate endpoint in clinical trials designed to test the hypothesis that interventions that delay the onset of aging-related diseases confer health benefits, for this model shows that resilience is accurately measured and predictively used. In addition, interventions that increase resilience might lead to treatments aimed at enhancing recovery following acute illness, or preventing poor outcomes from medical interventions in older, clinical samples. As a meeting of basic and clinical researchers involved in investigation of measures of aging and countermeasures to counteract effects of interventions on resilience in mice were considered actual and potential outcomes for assessing physiological aging or as the mechanism of action for developing a better understanding of how to intervene and intervene where interventions were absent. Relevant experimental mammal models were included to assess the potential outcomes. This approach to focusing on a single physiological system, one of age, costs, reproducibility, clinical relevance, and feasibility of being represented in such a study. In conclusion, the results indicate that while resilience is an important area, very little is known or established. More research is needed in the near future to develop appropriate measures of resilience in animal models in vivo aging contexts. The preliminary set of tools needed for the parameters is discussed here, recognizing that this is a first attempt.

Keywords: Aging; Resilience; Health Span

Aging, Health, and Resilience

Aging is the biological aging factor for many of the diseases that account for the bulk of morbidity, mortality, and health costs in most of the world. Indeed, aging is not merely a “risk factor” for disease. In fact, it is extremely all risky factors by one or more measures of importance. A common misconception is that chronic age-related diseases are less severe (less severe), and therefore, chronic disease prevention is less effective in older adults than in young adults. However, this is not true, because the time is taken to damage to accumulate. Moreover, this important reason might be that younger age groups have other defenses against catastrophic events and the progression. With aging, these defense capabilities decline, contributing to the emergence of disease that manifest clinically. A few examples of diseases potentially affecting the elderly are osteoporosis. Data from the Framingham study indicate that being 70 years old is a risk factor in older adults, high levels of natural resistance and absence

Special Article

Report: NIA Workshop on Measures of Physiologic Resilience in Human Aging

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A Conceptual Model

**REAL-WORLD STRESSOR; e.g.:**
- Hip fracture
- Myocardial infarction
- Infection
- Chemotherapy
- Surgery
- Death of spouse/child
- Divorce
- Verbal/emotional abuse

**OUTCOMES; e.g.:**
- Survival
- Functional status
- Symptoms
- Indicators of health or disease
- Health-related quality of life
- Subjective well-being

**Physiologic/Behavioral Responses**

**Resiliencies**
A Conceptual Model

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**SIMULATED STRESSORS**
Simulated stressor can perturb the same response systems as a real-world stressor
An example

**REAL-WORLD STRESSOR**
- Infection (e.g., influenza)

**PHYSIOLOGIC/BEHAVIORAL RESPONSES**

**OUTCOMES**
- ↓ Survival
- Weakness, restricted activity
- Septicemia
- ↓ Health-related quality of life
- ↓ Subjective well-being
Simulated stressor can perturb the same response systems as a real-world stressor

**REAL-WORLD STRESSOR**

- Infection (e.g., influenza)

**OUTCOMES OF SIMULATED STRESSORS**

- Innate immune, adaptive immune, inflammatory markers
- Pulmonary function tests
- Cardiorespiratory function
- Coagulation markers
- Skin reactions
- Neurocognitive function

**SIMULATED STRESSORS**

- e.g., specific viral antigen
- generic antigen (LPS)
- vaccination

**Major systems perturbed:**
- Immune
- Pulmonary
- Cardiovascular
- Musculoskeletal
- CNS
- Others
Why Measure Resiliencies?

- Resiliencies are **clinically meaningful in themselves**: determine survival, maintenance of function, duration of illness, suitability for aggressive medical or surgical procedures.

- Better tests of resiliencies could **improve clinical management** of older patients, e.g., inform choice of treatments.

- Resilience measures can **predict future health outcomes** (short- and long-term).

- Insight into changes in resiliencies across the human lifespan could **reveal aging mechanisms** underlying decrements, as well as factors contributing to the maintenance of resilient phenotypes.

- Characterizing physiologic responses and their underlying cellular mechanisms could lead to the **identification of novel therapeutic targets and interventions to enhance resiliencies**.

- Better predictive tests for resilience could be used as **surrogate markers of intervention trials to improve resiliencies**.
What is resilience?

What is health?
Trans-NIH resilience working group